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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,679	05/12/2005	Johannes Pohlner	2335.0030001/SRL/KPQ	7233

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EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	**PAPER NUMBER**
1649	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,679	POHLNER ET AL.	
	Examiner	Art Unit	
	Stacey MacFarlane	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-5,9,10,12,13,16-19,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8,11,14,15 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group V, Claims 6-8, 11, 14-15 and 20-22, and "rab31 translation products (polypeptides)", in the reply filed on July 6, 2007 is acknowledged.

2. Claims 1-5, 9-10, 12-13, 16-19 and 23-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 6, 2007.

3. Claims 6-8, 11, 14, 15 and 20-22, in so far as they read on the elected species, are under examination in the instant Office Action.

Specification

4. The text of the Specification and Claims 11 and 21 are not in compliance with the requirements for Sequence Identifiers (see MPEP 2422.03). The appropriate format for sequence identifiers is SEQ ID NO: X, wherein "X" is the sequence number. Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 6-8, 14-15, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 6 is vague and indefinite in so far as it employs the term "rab31" as a limitation. This term as it appears in this claim is novel, and reference to a precise amino acid sequence identified by a proper SEQ ID NO: is not referenced, therefore one cannot determine the metes and bounds of "rab31". Moreover, because the instant specification does not identify the property or combination of properties which is unique to and, therefore, definitive of a "rab31", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

8. Claim 6 is vague and indefinite for omitting essential elements. The claim recites "contacting a cell with a test compound" to screen for modulators of rab31. The relationship between the claimed elements, "rab31" and "a cell" is not obvious. Specifically, it is unclear if the "cell" being contacted is a cell that even expresses "a translation product of a gene coding for rab31".

9. Claim 7 is vague and indefinite for its recitation of a "test animal which is predisposed to developing ...a neurodegenerative disease or related diseases or disorders" and "a matched control animal which is predisposed to developing ... a neurodegenerative disease or related diseases or disorders". Claim 7 is incomplete for omitting the essential elements and/or active steps by which an animal is identified as

predisposed to disease. Such omission amounts to a gap between the elements. See MPEP § 2172.01.

10. Claims 8, 14-15, and 20 are indefinite for depending from indefinite claims.

Claim Rejections - 35 USC § 112, first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 6-8, 11, 14-15 and 20-22, are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 6 recites and "a fragment, or derivative, or variant of [a translation product of a gene coding for rab31]". Claims 7, 8, 11, 14-15 and 20-22 are dependent from Claim 6. The claims do not require that the "a fragment, or derivative, or variant of [a translation product of a gene coding for rab31]" possess any particular conserved structure or other disclosed distinguishing feature. Thus the claims are encompass a genus of molecules defined loosely as "a fragment, or derivative, or variant". Since the instant specification fails to describe the entire genus of molecules that are encompassed by these claims the instant disclosure fails to describe the genus, in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant knows of two specific examples of "a fragment, or derivative, or variant of [a translation product of a gene coding for rab31]" identified as GenBank accession number Q13636 and GenBank accession number AF183421 (Paragraph 0017). The claims, however, encompass method of screening for a modulator of fragments, derivatives or variants which have no relevance to rab31 as they are not limited to specific molecules with known structure.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, there is not even identification of any particular portion of the structure that must be conserved for rab31 activity. As stated above, it is not even clear what molecules are fragments, derivatives or variants that retain the activity of rab31, except GenBank accession number Q13636 and GenBank accession number AF183421. The specification does not provide a complete structure of either or these variants and fails to provide a representative number of species for the recited

genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of fragments, derivatives, or variants of a translation product of a gene coding for rab31, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires more than a mere recitation of an activity as part of the invention and a reference to a potential method of isolating or screening. The compound itself is required. See *Fiers v Revel*, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Only claims that encompass the full length of "a translation product of a gene coding for rab31" meet the written description proviso of 35 U.S.C. 112, first paragraph.

13. Claims 6-8, 11, 14-15 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112, 1st paragraph, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include:

(1) Nature of the invention
(2) Breadth of the claims
(3) Amount of direction or guidance presented
(4) Presence or absence of working examples
(5) State of the prior art
(6) Relative skill of those in the art
(7) Quantity of experimentation necessary, and
(8) Level of predictability in the art

The claims are drawn to in vitro and in vivo screening methods for a modulator of a neurodegenerative disease, related disease or disorder by identifying agents that

modulate the level and/or activity of any polypeptide shown in SEQ ID NO: 1, and include screening methods performed in rab31 transgenic animals.

The instant specification fails to defines any specific biologically activity mediated by the "translation product of a gene coding for rab31"of the claims. As for modulation of the expression levels of rab31, the instant disclosure describes a differential gene expression in human Alzheimer's disease brain samples by screening by a DNA biochip assay. However, one of ordinary skill in the art would easily recognize that the expression levels of many transcripts or proteins are measurably altered in a disease or pathological state. Since the disclosure has not provided evidence of a specific activity for rab31, there is no reasonable evidence that demonstrates a nexus between rab31 levels and neurodegenerative diseases or related disorders.

Furthermore, the disclosure has provided no guidance as to any potential test compounds to be screened by the method, and no direction in the form of a working example of any specific test compound screened by the method. Taken together with a lack of specific biological activity for rab31, there is no evidence that any modulator identified would reasonably serve as a modulator of neurodegenerative diseases, or related diseases or disorders.

The following reference demonstrates the current state of the art with respect to drug discovery screening in neurodegenerative diseases (Shaw et al. Nature Reviews/ Drug Discovery 6(4): 295-303, published April 2007). The reference states that while differentially expressed proteins have been identified in genetically-inherited forms of Alzheimer's disease (AD), further testing is required to link these biomarkers to

fundamental features of AD neuropathology, validate the biomarker within neuropathologically confirmed cases, and then identify the biomarker as distinguishing AD over other forms of dementia (page 297, last paragraph). The reference points out that, to date, no "disease-modifying therapies" have been identified from correlative biomarkers (page 301, **Future directions**).

Furthermore, the claimed method encompasses the use of an animal "which expresses a gene coding for rab31 ... under the control of a transcriptional control element which is not the native rab31 gene transcriptional control element". The instant specification has provided no guidance to one of ordinary skill in the art as to how to make and/or use the transgenic animal of the claims. As the following reference teaches, the development of a transgenic animal is not trivial and much unpredictability remains with respect to heterologous expression of genes(Ristevski, Molecular Biotechnology, 29: 153-163, February 2005). The reference sites specific problems of interfering transcripts (page 158, Section 3.2) and subsequent translation into protein (page 159, Section 3.4). The disclosure provides no direction as to how one of ordinary skill in the art would use the method wherein the animal was a transgenic animal.

In conclusion, since there is no guidance as to the claimed rab31 activity to be measured, no evidence that rab31 plays a functional role in the neuropathology of AD, and no example of a any test compound identified as a modulator of rab31, then it is concluded that the mere correlative evidence provided in the disclosure is an invitation to further experimentation. One of ordinary skill in the art would have to perform undue experimentation in order to use the invention of the claims.

Conclusion

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on Monday-Thursday 6:30AM-4:00 PM & ALT. Fridays, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

SNM

OLGA N. CHERNYSHEV, PH.D.
PRIMARY EXAMINER